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Effect of rapid timed injection in various phases of cardiac cycle on value of aortic regurgitation in man estimated by indicator dilution technique

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Timed injection above the aortic valve in the various phases of cardiac cycle produced variable results of aortic regurgitation estimated by the dye dilution technique in man. Highest values were obtained by end systolic or early diastolic injections and lowest values by end diastolic or early systolic injections.

This study confirmed the earlier findings in animal experiments and postulated in man, and also explains the inconsistent results of aortic regurgitation estimated by dye dilution using instant injection technique.

Injection of indicator downstream to the aortic valve and immediately sampling it upstream in the left ventricle can be used for detecting and quantitating aortic regurgitation (Malooly *et al.*, 1963). However, it has been shown in animal experiments that if the injection period is short and is actuated during the various phases of cardiac cycle, variable results of aortic regurgitation are obtained, being highest when injection is triggered at end systole or early diastole and lowest at end diastole or early systole (Armelin *et al.*, 1963). The effect of rapid injection of dye in various phases of cardiac cycle, on the value of aortic regurgitation, has not been reported in man, and it is the purpose of this communication to report such a study.

Methods

By percutaneous technique, via right femoral vein, a grey Kifa catheter (sampling catheter) was introduced transseptally into the left ventricle with its tip close to its apex. A red Kifa pigtail catheter (injecting catheter), with six side-holes, was introduced into the left ventricle retrogradely and later withdrawn and positioned 1 cm and 4 cm above the aortic valve, aided by pressure monitoring (Fig. 1). The tip of the injecting catheter was occluded with a metal tip occluder and the position of both the injecting and sampling catheter tips was recorded on the video-tape during every injection to detect whether any change of position occurred during the investigation. In addition, via the right femoral vein, a No. 7 Cournand catheter was introduced into the pulmonary artery and a short thin Teflon sampling catheter into the right femoral artery, and these were used for estimating cardiac output.

Cardiogreen, 0·5 ml, was used for every injection and the dye curve was obtained using Gilford densitometer Model 103-IR, Gilford infusion – withdrawal pump model 105-S and Kipp Zonen micrograph recorder model B-5. Suction speed was 28 ml/min and dynamic calibration was used (Sparling *et al.*, 1960; Shinebourne, Fleming, and Hamer, 1967).

Aortic regurgitation was estimated by injecting into ascending aorta above the aortic valve and sampling from the left ventricle. Immediately cardiac output was obtained by injecting into the pulmonary artery and sampling from femoral artery. The aortic regurgitation fraction is obtained by dividing the left ventricular dye curve area (LV_A) by femoral artery dye curve area (FA_A). Aortic regurgitation flow can be thus deduced,

$$QR = \frac{LV_A}{FA_A} \times \frac{QS}{\left(\frac{1-LV_A}{FA_A}\right)},$$

where QR = aortic regurgitation flow; and QS = cardiac output.

Rapid injection of the indicator was accomplished by introducing the dye into the injecting catheter (red Kifa) via side needle connected to the catheter assembly by a Y – stopcock, (Fig. 2) and flushing rapidly with a power injector (Contrac II) which can be triggered by the R wave of the electrocardiogram to start the injection at any cardiac phase selected.

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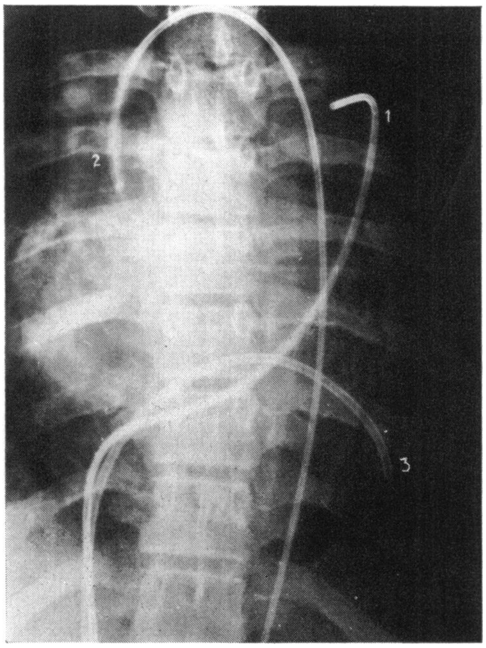


FIG. 1 *Catheters in position for regurgitation measurement. 1 Cournand No. 7 catheter in the main pulmonary artery; 2 injection catheter in the ascending aorta 4 cm above aortic valve; and 3 sampling catheter in the left ventricle.*

The characteristics of the instruments were first studied. The speed of the power injector of 30 ml per second was first examined. As the period of injection can be recorded on a multichannel recorder (Mingograph – 81), the time of injection of 30 ml fluid could be estimated by the time marker of the recorder, and the speed of injection was found to average 29·8 ml/sec. Then, the time interval between the beginning of injection and the appearance of dye from the tip of the injecting catheter and also the duration from the time of the arrival of the dye to the catheter tip to its complete evacuation from the catheter assembly, were estimated. This was performed in the following way: 0·5 ml (2·5 mg) Cardiogreen was introduced into the injecting catheter assembly (total volume = 1·7 ml) and different volumes of flushing fluid were used beginning from 1 ml to 6 ml. Each injectate was collected in a 100 ml flask and diluted with distilled water to 100 ml and the dye concentration was estimated by photometer (Hilger Model H 810–1) using 700 mμ filter. With 1 ml flushing fluid, only 7 per cent of the dye was cleared from the injection catheter assembly, while 1·5 ml flushing fluid caused expulsion of 87 per cent of the dye, and only 2 ml of flushing fluid was required to completely evacuate 100 per cent of the dye. As shown in Fig. 3, the duration of the beginning of injection and the appearance of dye at catheter tip was 30 msec, and the duration of the evacuation of dye was 20 msec and the total duration from the beginning of injection to the complete evacuation of dye from the catheter system was 50 msec.

Material

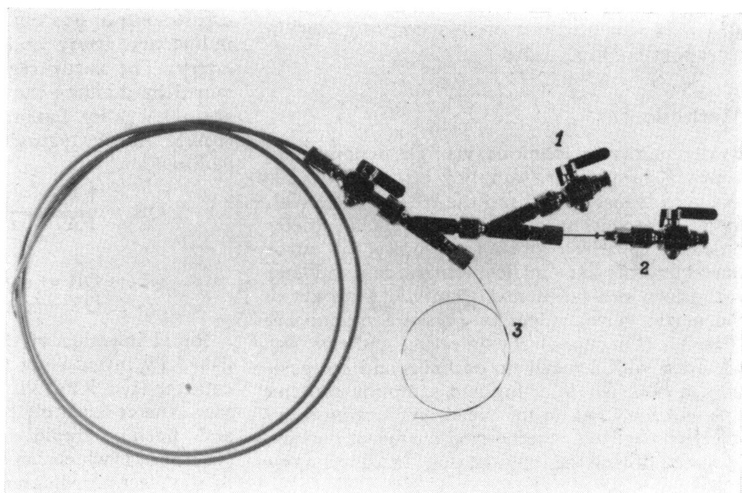
In all, 48 estimations of aortic regurgitation were performed in 5 male patients. The age distribution and the valvular lesions of each patient are shown in Table 1.

Omnopon 20 mg and hyoscine 0·4 mg were given as premedication, and the patients were asleep during most of the investigations. Additional pethidine (25 mg I.V.) was given occasionally if the patient was restless at the beginning of the investigation. An essential condition to a satisfactory study is that the heart rate must be stable during the investigation or else the factor of varying heart rate on aortic regurgitation (Warner and Toronto, 1961) would prevent any meaningful study.

Results

The results of the investigations are summarized in Table 2. In the first 3 cases (Fig. 4) in which the injection of dye for estimating aortic regurgitation was timed to occur at the beginning of systole and diastole, the value of aortic regurgitation was found to be consistently lower when the injection was limited to the beginning of systole and higher at the beginning of diastole. The injecting catheter was 1 cm above the aortic valve in all the investigations, and in addition in Case 3 it was also placed 4 cm above the aortic valve.

FIG. 2 *Injection catheter assembly. 1 stopcock connexion to power injector; 2 stopcock connected to needle for the introduction of dye; and 3 tip occluder.*



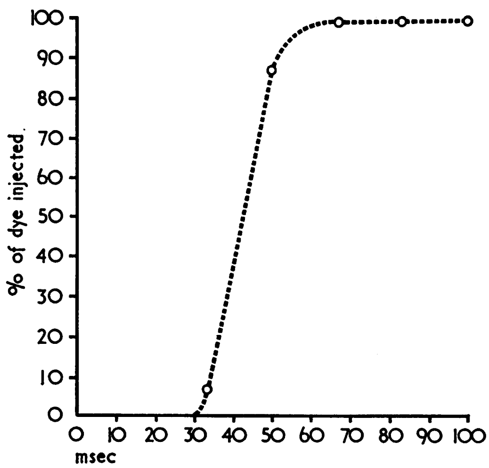


FIG. 3 *The duration of injection plotted against the injectate (%). It is clearly seen that the catheter delay is 30 msec and evacuation of dye was completed in 50 msec.*

In Case 4 (Fig. 5), in addition to early systolic and early diastolic injections, end diastolic injections were also performed. The difference between early systolic (25·3%) and early diastolic values (28·5%) of aortic regurgitation, with injection 1 cm above aortic valve, was minimal, but when early diastolic (28·5%) and late diastolic values (16%) are compared, the difference is more obvious. When injection is 4 cm above aortic valve, the early diastolic value is 24·3 per cent while

FIG. 4 *The values of aortic regurgitation (%) obtained during early diastolic and early systolic injections in Cases 1–3. The injection catheter is 1 cm above the aortic valve in all cases and, in addition, in Case 3 (closed circle) the injection catheter was also 4 cm above aortic valve.*

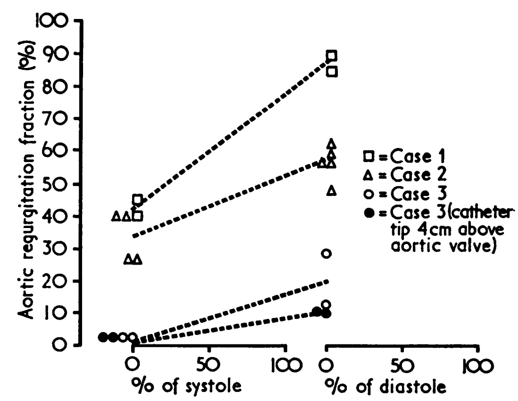


TABLE 1 *Age, sex, and valvular pathology of 5 cases studied*

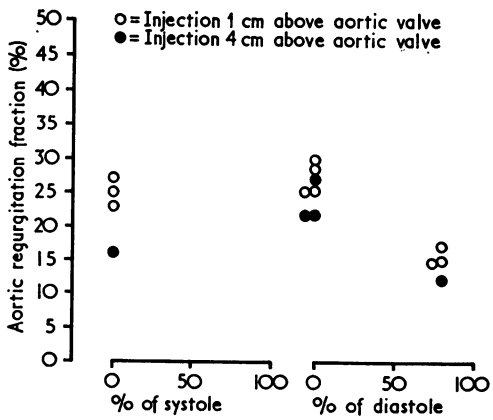
Case No.	*Age (yr)*	*Sex*	*Cardiac lesion*
1	20	M	Severe aortic regurgitation
2	28	M	Severe mitral stenosis Mild aortic regurgitation
3	25	M	Moderately severe aortic regurgitation
4	24	M	Moderate aortic stenosis Moderate aortic regurgitation
5	27	M	Severe aortic regurgitation

early systolic value is 16·3 per cent and end diastolic value is 12 per cent.

In Case 5 (Fig. 6) where injection in the various phases of diastole and systole was performed, it can be seen that, as in previous cases, early diastolic value of aortic regurgitation is higher than early systolic value, but the highest value of aortic regurgitation was obtained when injection was timed to occur in mid systole and lowest in two-thirds diastole. If the values of aortic regurgitation obtained by the injection in various phases of cardiac cycle 1 cm above aortic valve are plotted with the early systolic value normalized to 100 per cent (Fig. 7) the cyclic variation of aortic regurgitant fraction can be visualized.

When the mean and normalized early systolic and early diastolic values of all 5 patients in the two different catheter positions of injection (position A = 1 cm above aortic valve, position B = 4 cm above aortic valve) are compared (Table 3) it can be seen that the difference is 68 per cent for position A (5 patients) and 127 per cent for position B (3 patients). The difference is more significant if mid systolic values are compared with end

FIG. 5 *Case 4. Values of aortic regurgitation obtained by early and late diastolic and early systolic injection in two catheter positions.*



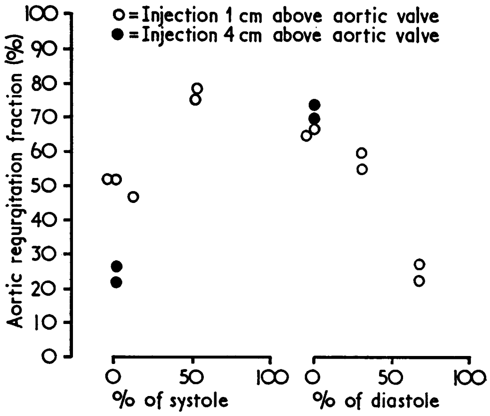


FIG. 6 *Case 5. Values of aortic regurgitation obtained in the various phases of cardiac cycle in two catheter positions.*

diastolic values as in Case 5 where it is nearly 200 per cent if end diastolic value is normalized to 100 per cent. A typical example of the dye curves obtained during the study is shown in Fig. 8.

Discussion

Since the introduction of upstream sampling technique in 1956 (Wood *et al.*, 1956), experimental studies have shown it to be useful in assessing aortic regurgitation (Malooly *et al.*, 1963; Armelin *et al.*, 1963). However, estimation of aortic regurgitation in man from left ventricular dilution curves, with randomly timed injection of indicator at aortic root, had produced inconsistent results (Frank *et al.*, 1966). It was felt that this inconsistency was probably due to critical dependance on the timing of the injection in the various phases of cardiac cycle, variation of heart rate, and varying sampling and injections sites (Frank *et al.*). The critical dependance of the value of aortic regurgitation to the timing of injection of dye in various phases of cardiac cycle had been well shown in animal experiments (Armelin *et al.*, 1963). However, though it had been postulated in men, it has not been studied so far. In the present study, timed injection of the dye into the aortic root in man produced similar varying results of aortic regurgitation, as found in experimental animals. Consistently higher values of aortic regurgitation were found when injection was timed to occur in late systole or the beginning of diastole and

FIG. 7 *Case 5. Values of aortic regurgitation plotted against the cardiac cycle, with the systolic value normalized to 100 per cent.*

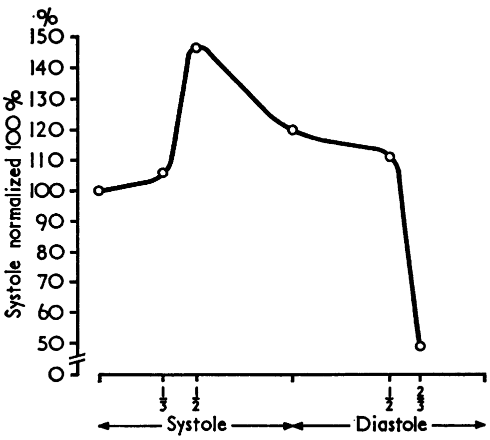


TABLE 2 *Aortic regurgitation fraction values (%) obtained by timed injection in various phases of cardiac cycle*

Case No.	Position of injecting catheter	Phase of injection Mid diastole	End diastole	Systole	One-third systole	Mid systole	Diastole
1	A			44·5			85
				40			90
	A			5			28
				5			13
2				5			—
	B			5			11
				5			11
	A			28·3			62
				28·3			48
3				40·0			57·2
				40			60
				—			57·2
	A		17·8	23·5			29
			15·2	25			27·5
			15·0	27·3			30
4			—	—			27·3
	B		12·6	16·3			22·9
							28
							22
	A	60	27·6	52	46·3	76·5	67·5
5		56·5	22·3	52	63·5	76·5	67·5
	B			26·5			72
				22			70

Position A = 1 cm above aortic valve; position B = 4 cm above aortic valve.

TABLE 3 *Mean and normalized values of aortic regurgitation of 5 patients in catheter position A (1 cm above aortic valve) and 3 patients in position B (4 cm above aortic valve)*

Catheter position	Phase	Systole	Diastole
A	Mean	29·7	49·9
	Normalized	100·0	168·0
B	Mean	14·9	33·8
	Normalized	100·0	227·0

lower values were found in late diastole or the beginning of systole. The lowest value was obtained with end diastolic injection and the highest value in mid systolic injection. In the present study, the heart rate remained constant and the effect of varying the site of sampling catheter was not studied and will be the subject of future study.

Theoretically, such variation is not unexpected as regurgitation of blood into the left ventricle in aortic regurgitation takes places only during diastole.

For the ideal value of aortic regurgitation to be obtained, the injection of dye should be confined to the systolic ejection period, with its speed proportion to the left ventricular ejection rate so that optimal mixing of dye is obtained. When diastole begins, the dye concentration of regurgitant flow is ideally mixed, and the left ventricle dye curve represents the ideal value for estimating aortic regurgitation. When injection is timed to occur in diastole, too much of the dye is washed into the left ventricle, with no opportunity for ideal mixing to take place at the aortic root and hence a falsely high value is obtained. With rapid injection in the beginning of systole, mixing nearer to the ideal uniform value is obtained, and blood regurgitating into the left ventricle during diastole is less likely to be mixed with too much dye as in diastolic injection. It has been suggested from animal experiments that to overcome this problem, the injection period should be prolonged to cover one to two cardiac cycles (Armelin *et al.*, 1963). Other centres have used the continuous infusion technique (Frank *et al.*, 1966) to overcome this problem, but still the problem of too much dye mixing with blood in diastole and regurgitating into the left ventricle is present. In our opinion the rapid injection method timed to occur in the beginning of systole gives a value of aortic regurgitation nearer to the true value and is simple, reproducible, and should be used when facilities are available.

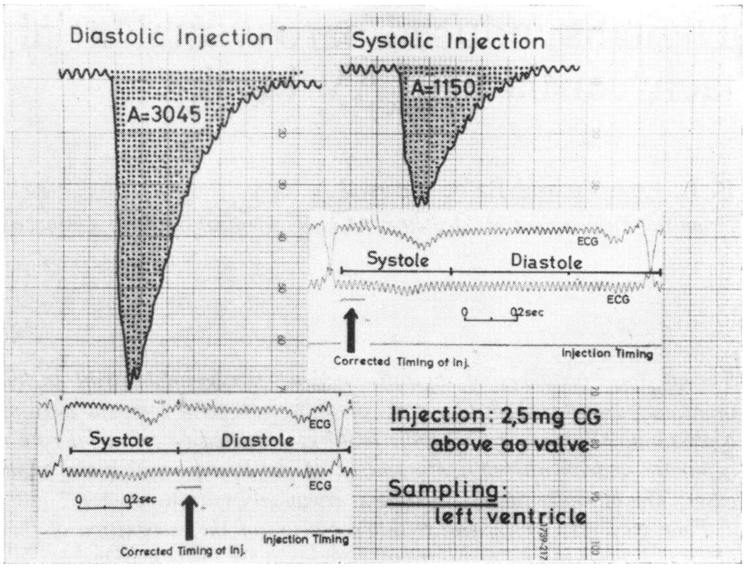


FIG. 8 *The upper left area shows the left ventricular dye curve during early diastolic injection at catheter position 4 cm above aortic valve, while the upper right area shows the dye curve area obtained by early systolic injection. The systolic area is about one-third of the diastolic area. The lower two tracings show the triggering recording which is corrected for catheter delay (30 msec).*

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